SEQUENCE LISTING

<110> Borean Pharma A/S

<120> Cleavage of fusion proteins using Granzyme B protease

<130> 3106

<160> 57

<170> PatentIn version 3.2

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<213> Artificial

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Met Gly Ser Ile Glu Gly Arg Ile Ile Gly Gly His Glu Ala Lys Pro
1 5 10 15

His Ser Arg Pro Tyr Met Ala Tyr Leu Met Ile Trp Asp Gln Lys Ser
20 25 30

Leu Lys Arg Cys Gly Gly Phe Leu Ile Gln Asp Asp Phe Val Leu Thr
35 40 45

Ala Ala His Cys Trp Gly Ser Ser Ile Asn Val Thr Leu Gly Ala His
50 55 60

Asn Ile Lys Glu Gln Glu Pro Thr Gln Gln Phe Ile Pro Val Lys Arg
65 70 75 80

Pro Ile Pro His Pro Ala Tyr Asn Pro Lys Asn Phe Ser Asn Asp Ile
85 90 95

Met Leu Leu Gln Leu Glu Arg Lys Ala Lys Arg Thr Arg Ala Val Gln
100 105 110

Pro Leu Arg Leu Pro Ser Asn Lys Ala Gln Val Lys Pro Gly Gln Thr
115 120 125

Cys Ser Val Ala Gly Trp Gly Gln Thr Ala Pro Leu Gly Lys His Ser
130 135 140

```
His Thr Leu Gln Glu Val Lys Met Thr Val Gln Glu Asp Arg Lys Cys
145                 150                 155                 160

Glu Ser Asp Leu Arg His Tyr Tyr Asp Ser Thr Ile Glu Leu Cys Val
                165                 170                 175

Gly Asp Pro Glu Ile Lys Lys Thr Ser Phe Lys Gly Asp Ser Gly Gly
            180                 185                 190

Pro Leu Val Cys Asn Lys Val Ala Gln Gly Ile Val Ser Tyr Gly Arg
        195                 200                 205

Asn Asn Gly Met Pro Pro Arg Ala Cys Thr Lys Val Ser Ser Phe Val
    210                 215                 220

His Trp Ile Lys Lys Thr Met Lys Arg Tyr Leu Asn Ser His His His
225                 230                 235                 240

His His His
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<210> 2
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<400> 2

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Met Gly Ser Ile Glu Pro Asp Ile Ile Gly Gly His Glu Ala Lys Pro
1               5                   10                  15

His Ser Arg Pro Tyr Met Ala Tyr Leu Met Ile Trp Asp Gln Lys Ser
            20                  25                  30

Leu Lys Arg Cys Gly Gly Phe Leu Ile Gln Asp Asp Phe Val Leu Thr
        35                  40                  45

Ala Ala His Cys Trp Gly Ser Ser Ile Asn Val Thr Leu Gly Ala His
    50                  55                  60

Asn Ile Lys Glu Gln Glu Pro Thr Gln Gln Phe Ile Pro Val Lys Arg
65                  70                  75                  80
```

```
Pro Ile Pro His Pro Ala Tyr Asn Pro Lys Asn Phe Ser Asn Asp Ile
                85                  90                  95

Met Leu Leu Gln Leu Glu Arg Lys Ala Lys Arg Thr Arg Ala Val Gln
            100                 105                 110

Pro Leu Arg Leu Pro Ser Asn Lys Ala Gln Val Lys Pro Gly Gln Thr
        115                 120                 125

Cys Ser Val Ala Gly Trp Gly Gln Thr Ala Pro Leu Gly Lys His Ser
    130                 135                 140

His Thr Leu Gln Glu Val Lys Met Thr Val Gln Glu Asp Arg Lys Cys
145                 150                 155                 160

Glu Ser Asp Leu Arg His Tyr Tyr Asp Ser Thr Ile Glu Leu Cys Val
                165                 170                 175

Gly Asp Pro Glu Ile Lys Lys Thr Ser Phe Lys Gly Asp Ser Gly Gly
            180                 185                 190

Pro Leu Val Cys Asn Lys Val Ala Gln Gly Ile Val Ser Tyr Gly Arg
        195                 200                 205

Asn Asn Gly Met Pro Pro Arg Ala Cys Thr Lys Val Ser Ser Phe Val
    210                 215                 220

His Trp Ile Lys Lys Thr Met Lys Arg Tyr Leu Asn Ser His His His
225                 230                 235                 240

His His His
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<400> 3

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Met Gly Ser Ile Glu Ala Asp Ile Ile Gly Gly His Glu Ala Lys Pro
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1 5 10 15

His Ser Arg Pro Tyr Met Ala Tyr Leu Met Ile Trp Asp Gln Lys Ser
20 25 30

Leu Lys Arg Cys Gly Gly Phe Leu Ile Gln Asp Asp Phe Val Leu Thr
35 40 45

Ala Ala His Cys Trp Gly Ser Ser Ile Asn Val Thr Leu Gly Ala His
50 55 60

Asn Ile Lys Glu Gln Glu Pro Thr Gln Gln Phe Ile Pro Val Lys Arg
65 70 75 80

Pro Ile Pro His Pro Ala Tyr Asn Pro Lys Asn Phe Ser Asn Asp Ile
85 90 95

Met Leu Leu Gln Leu Glu Arg Lys Ala Lys Arg Thr Arg Ala Val Gln
100 105 110

Pro Leu Arg Leu Pro Ser Asn Lys Ala Gln Val Lys Pro Gly Gln Thr
115 120 125

Cys Ser Val Ala Gly Trp Gly Gln Thr Ala Pro Leu Gly Lys His Ser
130 135 140

His Thr Leu Gln Glu Val Lys Met Thr Val Gln Glu Asp Arg Lys Cys
145 150 155 160

Glu Ser Asp Leu Arg His Tyr Tyr Asp Ser Thr Ile Glu Leu Cys Val
165 170 175

Gly Asp Pro Glu Ile Lys Lys Thr Ser Phe Lys Gly Asp Ser Gly Gly
180 185 190

Pro Leu Val Cys Asn Lys Val Ala Gln Gly Ile Val Ser Tyr Gly Arg
195 200 205

Asn Asn Gly Met Pro Pro Arg Ala Cys Thr Lys Val Ser Ser Phe Val
210 215 220

His Trp Ile Lys Lys Thr Met Lys Arg Tyr Leu Asn Ser His His His
225 230 235 240

His His His

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<223> pro-IEPD-GrB-H6 C228S

<400> 4

Met Gly Ser Ile Glu Pro Asp Ile Ile Gly Gly His Glu Ala Lys Pro
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His Ser Arg Pro Tyr Met Ala Tyr Leu Met Ile Trp Asp Gln Lys Ser
20 25 30

Leu Lys Arg Cys Gly Gly Phe Leu Ile Gln Asp Asp Phe Val Leu Thr
35 40 45

Ala Ala His Cys Trp Gly Ser Ser Ile Asn Val Thr Leu Gly Ala His
50 55 60

Asn Ile Lys Glu Gln Glu Pro Thr Gln Gln Phe Ile Pro Val Lys Arg
65 70 75 80

Pro Ile Pro His Pro Ala Tyr Asn Pro Lys Asn Phe Ser Asn Asp Ile
85 90 95

Met Leu Leu Gln Leu Glu Arg Lys Ala Lys Arg Thr Arg Ala Val Gln
100 105 110

Pro Leu Arg Leu Pro Ser Asn Lys Ala Gln Val Lys Pro Gly Gln Thr
115 120 125

Cys Ser Val Ala Gly Trp Gly Gln Thr Ala Pro Leu Gly Lys His Ser
130 135 140

His Thr Leu Gln Glu Val Lys Met Thr Val Gln Glu Asp Arg Lys Cys
145 150 155 160

Glu Ser Asp Leu Arg His Tyr Tyr Asp Ser Thr Ile Glu Leu Cys Val

```
                165                 170                 175

Gly Asp Pro Glu Ile Lys Lys Thr Ser Phe Lys Gly Asp Ser Gly Gly
            180                 185                 190

Pro Leu Val Cys Asn Lys Val Ala Gln Gly Ile Val Ser Tyr Gly Arg
        195                 200                 205

Asn Asn Gly Met Pro Pro Arg Ala Ser Thr Lys Val Ser Ser Phe Val
    210                 215                 220

His Trp Ile Lys Lys Thr Met Lys Arg Tyr Leu Asn Ser His His His
225                 230                 235                 240

His His His
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<213> Artificial

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1               5                   10                  15

His Ser Arg Pro Tyr Met Ala Tyr Leu Met Ile Trp Asp Gln Lys Ser
            20                  25                  30

Leu Lys Arg Cys Gly Gly Phe Leu Ile Gln Asp Asp Phe Val Leu Thr
        35                  40                  45

Ala Ala His Cys Trp Gly Ser Ser Ile Asn Val Thr Leu Gly Ala His
    50                  55                  60

Asn Ile Lys Glu Gln Glu Pro Thr Gln Gln Phe Ile Pro Val Lys Arg
65                  70                  75                  80

Pro Ile Pro His Pro Ala Tyr Asn Pro Lys Asn Phe Ser Asn Asp Ile
                85                  90                  95
```

```
Met Leu Leu Gln Leu Glu Arg Lys Ala Lys Arg Thr Arg Ala Val Gln
            100                 105                 110

Pro Leu Arg Leu Pro Ser Asn Lys Ala Gln Val Lys Pro Gly Gln Thr
        115                 120                 125

Cys Ser Val Ala Gly Trp Gly Gln Thr Ala Pro Leu Gly Lys His Ser
    130                 135                 140

His Thr Leu Gln Glu Val Lys Met Thr Val Gln Glu Asp Arg Lys Cys
145                 150                 155                 160

Glu Ser Asp Leu Arg His Tyr Tyr Asp Ser Thr Ile Glu Leu Cys Val
                165                 170                 175

Gly Asp Pro Glu Ile Lys Lys Thr Ser Phe Lys Gly Asp Ser Gly Gly
            180                 185                 190

Pro Leu Val Cys Asn Lys Val Ala Gln Gly Ile Val Ser Tyr Gly Arg
        195                 200                 205

Asn Asn Gly Met Pro Pro Arg Ala Ala Thr Lys Val Ser Ser Phe Val
    210                 215                 220

His Trp Ile Lys Lys Thr Met Lys Arg Tyr Leu Asn Ser His His His
225                 230                 235                 240

His His His
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<213> Artificial

<220>
<223> pro-IEPD-GrB-H6 C228T

<400> 6

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His Ser Arg Pro Tyr Met Ala Tyr Leu Met Ile Trp Asp Gln Lys Ser
            20                  25                  30
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```
Leu Lys Arg Cys Gly Gly Phe Leu Ile Gln Asp Asp Phe Val Leu Thr
        35                  40                  45

Ala Ala His Cys Trp Gly Ser Ser Ile Asn Val Thr Leu Gly Ala His
    50                  55                  60

Asn Ile Lys Glu Gln Glu Pro Thr Gln Gln Phe Ile Pro Val Lys Arg
65                  70                  75                  80

Pro Ile Pro His Pro Ala Tyr Asn Pro Lys Asn Phe Ser Asn Asp Ile
                85                  90                  95

Met Leu Leu Gln Leu Glu Arg Lys Ala Lys Arg Thr Arg Ala Val Gln
            100                 105                 110

Pro Leu Arg Leu Pro Ser Asn Lys Ala Gln Val Lys Pro Gly Gln Thr
        115                 120                 125

Cys Ser Val Ala Gly Trp Gly Gln Thr Ala Pro Leu Gly Lys His Ser
    130                 135                 140

His Thr Leu Gln Glu Val Lys Met Thr Val Gln Glu Asp Arg Lys Cys
145                 150                 155                 160

Glu Ser Asp Leu Arg His Tyr Tyr Asp Ser Thr Ile Glu Leu Cys Val
                165                 170                 175

Gly Asp Pro Glu Ile Lys Lys Thr Ser Phe Lys Gly Asp Ser Gly Gly
            180                 185                 190

Pro Leu Val Cys Asn Lys Val Ala Gln Gly Ile Val Ser Tyr Gly Arg
        195                 200                 205

Asn Asn Gly Met Pro Pro Arg Ala Thr Thr Lys Val Ser Ser Phe Val
    210                 215                 220

His Trp Ile Lys Lys Thr Met Lys Arg Tyr Leu Asn Ser His His His
225                 230                 235                 240

His His His
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<210> 7
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<213> Artificial

<220>
<223> pro-IEPD-GrB-H6 C228V

<400> 7

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1               5                  10                  15

His Ser Arg Pro Tyr Met Ala Tyr Leu Met Ile Trp Asp Gln Lys Ser
            20                  25                  30

Leu Lys Arg Cys Gly Gly Phe Leu Ile Gln Asp Asp Phe Val Leu Thr
        35                  40                  45

Ala Ala His Cys Trp Gly Ser Ser Ile Asn Val Thr Leu Gly Ala His
    50                  55                  60

Asn Ile Lys Glu Gln Glu Pro Thr Gln Gln Phe Ile Pro Val Lys Arg
65                  70                  75                  80

Pro Ile Pro His Pro Ala Tyr Asn Pro Lys Asn Phe Ser Asn Asp Ile
                85                  90                  95

Met Leu Leu Gln Leu Glu Arg Lys Ala Lys Arg Thr Arg Ala Val Gln
            100                 105                 110

Pro Leu Arg Leu Pro Ser Asn Lys Ala Gln Val Lys Pro Gly Gln Thr
        115                 120                 125

Cys Ser Val Ala Gly Trp Gly Gln Thr Ala Pro Leu Gly Lys His Ser
    130                 135                 140

His Thr Leu Gln Glu Val Lys Met Thr Val Gln Glu Asp Arg Lys Cys
145                 150                 155                 160

Glu Ser Asp Leu Arg His Tyr Tyr Asp Ser Thr Ile Glu Leu Cys Val
                165                 170                 175

Gly Asp Pro Glu Ile Lys Lys Thr Ser Phe Lys Gly Asp Ser Gly Gly
            180                 185                 190
```

Pro Leu Val Cys Asn Lys Val Ala Gln Gly Ile Val Ser Tyr Gly Arg
195 200 205

Asn Asn Gly Met Pro Pro Arg Ala Val Thr Lys Val Ser Ser Phe Val
210 215 220

His Trp Ile Lys Lys Thr Met Lys Arg Tyr Leu Asn Ser His His His
225 230 235 240

His His His

<210> 8
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<212> PRT
<213> Artificial

<220>
<223> pro-IEPD-GrB-H6 C228F

<400> 8

Met Gly Ser Ile Glu Pro Asp Ile Ile Gly Gly His Glu Ala Lys Pro
1 5 10 15

His Ser Arg Pro Tyr Met Ala Tyr Leu Met Ile Trp Asp Gln Lys Ser
20 25 30

Leu Lys Arg Cys Gly Gly Phe Leu Ile Gln Asp Asp Phe Val Leu Thr
35 40 45

Ala Ala His Cys Trp Gly Ser Ser Ile Asn Val Thr Leu Gly Ala His
50 55 60

Asn Ile Lys Glu Gln Glu Pro Thr Gln Gln Phe Ile Pro Val Lys Arg
65 70 75 80

Pro Ile Pro His Pro Ala Tyr Asn Pro Lys Asn Phe Ser Asn Asp Ile
85 90 95

Met Leu Leu Gln Leu Glu Arg Lys Ala Lys Arg Thr Arg Ala Val Gln
100 105 110

Pro Leu Arg Leu Pro Ser Asn Lys Ala Gln Val Lys Pro Gly Gln Thr
115 120 125

```
Cys Ser Val Ala Gly Trp Gly Gln Thr Ala Pro Leu Gly Lys His Ser
    130                 135                 140

His Thr Leu Gln Glu Val Lys Met Thr Val Gln Glu Asp Arg Lys Cys
145                 150                 155                 160

Glu Ser Asp Leu Arg His Tyr Tyr Asp Ser Thr Ile Glu Leu Cys Val
                165                 170                 175

Gly Asp Pro Glu Ile Lys Lys Thr Ser Phe Lys Gly Asp Ser Gly Gly
            180                 185                 190

Pro Leu Val Cys Asn Lys Val Ala Gln Gly Ile Val Ser Tyr Gly Arg
        195                 200                 205

Asn Asn Gly Met Pro Pro Arg Ala Phe Thr Lys Val Ser Ser Phe Val
    210                 215                 220

His Trp Ile Lys Lys Thr Met Lys Arg Tyr Leu Asn Ser His His His
225                 230                 235                 240

His His His
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<210> 9
<211> 46
<212> DNA
<213> Artificial

<220>
<223> H6 C-term fw

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<210> 10
<211> 46
<212> DNA
<213> Artificial

<220>
<223> H6 C-term rev

<400> 10
aattgcgtta gtgatggtga tggtgatgtg aattcaagct tccgct 46

<210> 11
<211> 40
<212> DNA
<213> Artificial

<220>
<223> GrBfw primer

<400> 11
catgggatcc atcgagggta ggatcatcgg gggacatgag 40

<210> 12
<211> 38
<212> DNA
<213> Artificial

<220>
<223> GrBrev EcoRI primer

<400> 12
gcgtgaattc aggtaccgtt tcatggtttt ctttatcc 38

<210> 13
<211> 715
<212> DNA
<213> Artificial

<220>
<223> GrB EcoRI fragment

<400> 13
catgggatcc atcgagggta ggatcatcgg gggacatgag gccaagcccc actcccgccc 60

ctacatggct tatcttatga tctgggatca gaagtctctg aagaggtgcg gtggcttcct 120

gatacaagac gacttcgtgc tgacagctgc tcactgttgg ggaagctcca taaatgtcac 180

cttgggggcc cacaatatca aagaacagga gccgacccag cagtttatcc ctgtgaaaag 240

acccatcccc catccagcct ataatcctaa gaacttctcc aacgacatca tgctactgca 300

gctggagaga aaggccaagc ggaccagagc tgtgcagccc ctcaggctac ctagcaacaa 360

ggcccaggtg aagccagggc agacatgcag tgtggccggc tgggggcaga cggccccccct 420

gggaaaacac tcacacacac tacaagaggt gaagatgaca gtgcaggaag atcgaaagtg 480

cgaatctgac ttacgccatt attacgacag taccattgag ttgtgcgtgg gggacccaga 540

gattaaaaag acttccttta agggggactc tggaggccct cttgtgtgta acaaggtggc 600

ccagggcatt gtctcctatg gacgaaacaa tggcatgcct ccacgagcct gcaccaaagt 660

ctcaagcttt gtacactgga taaagaaaac catgaaacgg tacctgaatt cacgc 715

<210> 14
<211> 33
<212> DNA
<213> Artificial

<220>
<223> GrB GR-PD fw

<400> 14
tccatcgagc cggatatcat cgggggacat gag 33

<210> 15
<211> 34
<212> DNA
<213> Artificial

<220>
<223> GrB GR-PD rev

<400> 15
ccccgatgat atccggctcg atggatccca tatg 34

<210> 16
<211> 33
<212> DNA
<213> Artificial

<220>
<223> GrB GR-AD fw

<400> 16
tccatcgagg ctgatatcat cgggggacat gag 33

<210> 17
<211> 34
<212> DNA
<213> Artificial

<220>
<223> GrB GR-AD rev

<400> 17
ccccgatgat atcagcctcg atggatccca tatg 34

<210> 18
<211> 27
<212> DNA
<213> Artificial

<220>
<223> GrB SAT fw

<400> 18
tccacgagca dccaccaaag tctcaag 27

<210> 19
<211> 26
<212> DNA
<213> Artificial

<220>
<223> GrB SAT rev

<400> 19
agactttggt gghggctcgt ggaggc 26

<210> 20
<211> 27
<212> DNA
<213> Artificial

<220>
<223> GrB VF fw

<400> 20
tccacgagcc ktcaccaaag tctcaag 27

<210> 21
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<223> GrB VF rev

<400> 21
agactttggt gamggctcgt ggaggc 26

<210> 22
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<213> Artificial

<220>
<223> H6-TripUB IEPD!SP

<400> 22

Met Gly Ser His His His His His His Gly Ser Gly Ser Gly Ser Ile
1 5 10 15

Glu Pro Asp Ser Pro Gly Thr Glu Pro Pro Thr Gln Lys Pro Lys Lys
20 25 30

```
Ile Val Asn Ala Lys Lys Asp Val Val Asn Thr Lys Met Phe Glu Glu
        35                  40                  45

Leu Lys Ser Arg Leu Asp Thr Leu Ala Gln Glu Val Ala Leu Leu Lys
    50                  55                  60

Glu Gln Gln Ala Leu Gln Thr Val Gly Ser Gln Ile Phe Val Lys Thr
65                  70                  75                  80

Leu Thr Gly Lys Thr Ile Thr Leu Glu Val Glu Pro Ser Asp Thr Ile
                85                  90                  95

Glu Asn Val Lys Ala Lys Ile Gln Asp Lys Glu Gly Ile Pro Pro Asp
            100                 105                 110

Gln Gln Arg Leu Ile Phe Ala Gly Lys Gln Leu Glu Asp Gly Arg Thr
        115                 120                 125

Leu Ser Asp Tyr Asn Ile Gln Lys Glu Ser Thr Leu His Leu Val Leu
    130                 135                 140

Arg Leu Arg Gly Gly Ser
145                 150
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<210> 23
<211> 338
<212> PRT
<213> Artificial

<220>
<223> H6-IEPD-RAP

<400> 23

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Met Gly Ser His His His His His His Gly Ser Ile Glu Pro Asp Tyr
1               5                   10                  15

Ser Arg Glu Lys Asn Gln Pro Lys Pro Ser Pro Lys Arg Glu Ser Gly
            20                  25                  30

Glu Glu Phe Arg Met Glu Lys Leu Asn Gln Leu Trp Glu Lys Ala Gln
        35                  40                  45

Arg Leu His Leu Pro Pro Val Arg Leu Ala Glu Leu His Ala Asp Leu
```

```
    50                  55                  60

Lys Ile Gln Glu Arg Asp Glu Leu Ala Trp Lys Lys Leu Lys Leu Asp
65                  70                  75                  80

Gly Leu Asp Glu Asp Gly Glu Lys Glu Ala Arg Leu Ile Arg Asn Leu
                85                  90                  95

Asn Val Ile Leu Ala Lys Tyr Gly Leu Asp Gly Lys Lys Asp Ala Arg
            100                 105                 110

Gln Val Thr Ser Asn Ser Leu Ser Gly Thr Gln Glu Asp Gly Leu Asp
        115                 120                 125

Asp Pro Arg Leu Glu Lys Leu Trp His Lys Ala Lys Thr Ser Gly Lys
    130                 135                 140

Phe Ser Gly Glu Glu Leu Asp Lys Leu Trp Arg Glu Phe Leu His His
145                 150                 155                 160

Lys Glu Lys Val His Glu Tyr Asn Val Leu Leu Glu Thr Leu Ser Arg
                165                 170                 175

Thr Glu Glu Ile His Glu Asn Val Ile Ser Pro Ser Asp Leu Ser Asp
            180                 185                 190

Ile Lys Gly Ser Val Leu His Ser Arg His Thr Glu Leu Lys Glu Lys
        195                 200                 205

Leu Arg Ser Ile Asn Gln Gly Leu Asp Arg Leu Arg Arg Val Ser His
    210                 215                 220

Gln Gly Tyr Ser Thr Glu Ala Glu Phe Glu Glu Pro Arg Val Ile Asp
225                 230                 235                 240

Leu Trp Asp Leu Ala Gln Ser Ala Asn Leu Thr Asp Lys Glu Leu Glu
                245                 250                 255

Ala Phe Arg Glu Glu Leu Lys His Phe Glu Ala Lys Ile Glu Lys His
            260                 265                 270

Asn His Tyr Gln Lys Gln Leu Glu Ile Ala His Glu Lys Leu Arg His
        275                 280                 285
```

Ala Glu Ser Val Gly Asp Gly Glu Arg Val Ser Arg Ser Arg Glu Lys
290 295 300

His Ala Leu Leu Glu Gly Arg Thr Lys Glu Leu Gly Tyr Thr Val Lys
305 310 315 320

Lys His Leu Gln Asp Leu Ser Gly Arg Ile Ser Arg Ala Arg His Asn
325 330 335

Glu Leu

<210> 24
<211> 336
<212> PRT
<213> Artificial

<220>
<223> H6Ubi-IEPD-ApoA1

<400> 24

Met Gly Ser His His His His His His Gly Ser Gln Ile Phe Val Lys
1 5 10 15

Thr Leu Thr Gly Lys Thr Ile Thr Leu Glu Val Glu Pro Ser Asp Thr
20 25 30

Ile Glu Asn Val Lys Ala Lys Ile Gln Asp Lys Glu Gly Ile Pro Pro
35 40 45

Asp Gln Gln Arg Leu Ile Phe Ala Gly Lys Gln Leu Glu Asp Gly Arg
50 55 60

Thr Leu Ser Asp Tyr Asn Ile Gln Lys Glu Ser Thr Leu His Leu Val
65 70 75 80

Leu Arg Leu Arg Gly Gly Ser Ile Glu Pro Asp Gly Gly Asp Glu Pro
85 90 95

Pro Gln Ser Pro Trp Asp Arg Val Lys Asp Leu Ala Thr Val Tyr Val
100 105 110

Asp Val Leu Lys Asp Ser Gly Arg Asp Tyr Val Ser Gln Phe Glu Gly

```
        115                 120                 125

Ser Ala Leu Gly Lys Gln Leu Asn Leu Lys Leu Leu Asp Asn Trp Asp
    130                 135                 140

Ser Val Thr Ser Thr Phe Ser Lys Leu Arg Glu Gln Leu Gly Pro Val
145                 150                 155                 160

Thr Gln Glu Phe Trp Asp Asn Leu Glu Lys Glu Thr Glu Gly Leu Arg
                165                 170                 175

Gln Glu Met Ser Lys Asp Leu Glu Glu Val Lys Ala Lys Val Gln Pro
            180                 185                 190

Tyr Leu Asp Asp Phe Gln Lys Lys Trp Gln Glu Glu Met Glu Leu Tyr
        195                 200                 205

Arg Gln Lys Val Glu Pro Leu Arg Ala Glu Leu Gln Glu Gly Ala Arg
    210                 215                 220

Gln Lys Leu His Glu Leu Gln Glu Lys Leu Ser Pro Leu Gly Glu Glu
225                 230                 235                 240

Met Arg Asp Arg Ala Arg Ala His Val Asp Ala Leu Arg Thr His Leu
                245                 250                 255

Ala Pro Tyr Ser Asp Glu Leu Arg Gln Arg Leu Ala Ala Arg Leu Glu
            260                 265                 270

Ala Leu Lys Glu Asn Gly Gly Ala Arg Leu Ala Glu Tyr His Ala Lys
        275                 280                 285

Ala Thr Glu His Leu Ser Thr Leu Ser Glu Lys Ala Lys Pro Ala Leu
    290                 295                 300

Glu Asp Leu Arg Gln Gly Leu Leu Pro Val Leu Glu Ser Phe Lys Val
305                 310                 315                 320

Ser Phe Leu Ser Ala Leu Glu Glu Tyr Thr Lys Lys Leu Asn Thr Gln
                325                 330                 335
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<210> 25
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<212> PRT
<213> Artificial

<220>
<223> H6-IEPD-TN123

<400> 25

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Met Gly Ser His His His His His His Gly Ser Ile Glu Pro Asp Gly
1               5                  10                  15

Glu Pro Pro Thr Gln Lys Pro Lys Lys Ile Val Asn Ala Lys Lys Asp
            20                  25                  30

Val Val Asn Thr Lys Met Phe Glu Glu Leu Lys Ser Arg Leu Asp Thr
        35                  40                  45

Leu Ala Gln Glu Val Ala Leu Leu Lys Glu Gln Gln Ala Leu Gln Thr
    50                  55                  60

Val Cys Leu Lys Gly Thr Lys Val His Met Lys Cys Phe Leu Ala Phe
65                  70                  75                  80

Thr Gln Thr Lys Thr Phe His Glu Ala Ser Glu Asp Cys Ile Ser Arg
                85                  90                  95

Gly Gly Thr Leu Ser Thr Pro Gln Thr Gly Ser Glu Asn Asp Ala Leu
            100                 105                 110

Tyr Glu Tyr Leu Arg Gln Ser Val Gly Asn Glu Ala Glu Ile Trp Leu
        115                 120                 125

Gly Leu Asn Asp Met Ala Ala Glu Gly Thr Trp Val Asp Met Thr Gly
    130                 135                 140

Ala Arg Ile Ala Tyr Lys Asn Trp Glu Thr Glu Ile Thr Ala Gln Pro
145                 150                 155                 160

Asp Gly Gly Lys Thr Glu Asn Cys Ala Val Leu Ser Gly Ala Ala Asn
                165                 170                 175

Gly Lys Trp Phe Asp Lys Arg Cys Arg Asp Gln Leu Pro Tyr Ile Cys
            180                 185                 190

Gln Phe Gly Ile Val
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195

<210> 26
<211> 150
<212> PRT
<213> Artificial

<220>
<223> H6-TripUB IQAD!SP

<400> 26

Met Gly Ser His His His His His His Gly Ser Gly Ser Gly Ser Ile
1 5 10 15

Gln Ala Asp Ser Pro Gly Thr Glu Pro Pro Thr Gln Lys Pro Lys Lys
20 25 30

Ile Val Asn Ala Lys Lys Asp Val Val Asn Thr Lys Met Phe Glu Glu
35 40 45

Leu Lys Ser Arg Leu Asp Thr Leu Ala Gln Glu Val Ala Leu Leu Lys
50 55 60

Glu Gln Gln Ala Leu Gln Thr Val Gly Ser Gln Ile Phe Val Lys Thr
65 70 75 80

Leu Thr Gly Lys Thr Ile Thr Leu Glu Val Glu Pro Ser Asp Thr Ile
85 90 95

Glu Asn Val Lys Ala Lys Ile Gln Asp Lys Glu Gly Ile Pro Pro Asp
100 105 110

Gln Gln Arg Leu Ile Phe Ala Gly Lys Gln Leu Glu Asp Gly Arg Thr
115 120 125

Leu Ser Asp Tyr Asn Ile Gln Lys Glu Ser Thr Leu His Leu Val Leu
130 135 140

Arg Leu Arg Gly Gly Ser
145 150

<210> 27
<211> 150
<212> PRT
<213> Artificial

<220>
<223> H6-TripUB IQAD!SG

<400> 27

Met Gly Ser His His His His His His Gly Ser Gly Ser Gly Ser Ile
1 5 10 15

Gln Ala Asp Ser Gly Gly Thr Glu Pro Pro Thr Gln Lys Pro Lys Lys
20 25 30

Ile Val Asn Ala Lys Lys Asp Val Val Asn Thr Lys Met Phe Glu Glu
35 40 45

Leu Lys Ser Arg Leu Asp Thr Leu Ala Gln Glu Val Ala Leu Leu Lys
50 55 60

Glu Gln Gln Ala Leu Gln Thr Val Gly Ser Gln Ile Phe Val Lys Thr
65 70 75 80

Leu Thr Gly Lys Thr Ile Thr Leu Glu Val Glu Pro Ser Asp Thr Ile
85 90 95

Glu Asn Val Lys Ala Lys Ile Gln Asp Lys Glu Gly Ile Pro Pro Asp
100 105 110

Gln Gln Arg Leu Ile Phe Ala Gly Lys Gln Leu Glu Asp Gly Arg Thr
115 120 125

Leu Ser Asp Tyr Asn Ile Gln Lys Glu Ser Thr Leu His Leu Val Leu
130 135 140

Arg Leu Arg Gly Gly Ser
145 150

<210> 28
<211> 150
<212> PRT
<213> Artificial

<220>
<223> H6-TripUB VGPD!SP

<400> 28

Met Gly Ser His His His His His His Gly Ser Gly Ser Gly Ser Val

```
1               5                   10                  15

Gly Pro Asp Ser Pro Gly Thr Glu Pro Pro Thr Gln Lys Pro Lys Lys
            20                  25                  30

Ile Val Asn Ala Lys Lys Asp Val Val Asn Thr Lys Met Phe Glu Glu
        35                  40                  45

Leu Lys Ser Arg Leu Asp Thr Leu Ala Gln Glu Val Ala Leu Leu Lys
    50                  55                  60

Glu Gln Gln Ala Leu Gln Thr Val Gly Ser Gln Ile Phe Val Lys Thr
65                  70                  75                  80

Leu Thr Gly Lys Thr Ile Thr Leu Glu Val Glu Pro Ser Asp Thr Ile
                85                  90                  95

Glu Asn Val Lys Ala Lys Ile Gln Asp Lys Glu Gly Ile Pro Pro Asp
            100                 105                 110

Gln Gln Arg Leu Ile Phe Ala Gly Lys Gln Leu Glu Asp Gly Arg Thr
        115                 120                 125

Leu Ser Asp Tyr Asn Ile Gln Lys Glu Ser Thr Leu His Leu Val Leu
    130                 135                 140

Arg Leu Arg Gly Gly Ser
145                 150
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<210> 29
<211> 150
<212> PRT
<213> Artificial

<220>
<223> H6-TripUB VGPD!FG

<400> 29

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Met Gly Ser His His His His His His Gly Ser Gly Ser Gly Ser Val
1               5                   10                  15

Gly Pro Asp Phe Gly Gly Thr Glu Pro Pro Thr Gln Lys Pro Lys Lys
            20                  25                  30
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```
Ile Val Asn Ala Lys Lys Asp Val Val Asn Thr Lys Met Phe Glu Glu
        35                  40                  45

Leu Lys Ser Arg Leu Asp Thr Leu Ala Gln Glu Val Ala Leu Leu Lys
    50                  55                  60

Glu Gln Gln Ala Leu Gln Thr Val Gly Ser Gln Ile Phe Val Lys Thr
65                  70                  75                  80

Leu Thr Gly Lys Thr Ile Thr Leu Glu Val Glu Pro Ser Asp Thr Ile
                85                  90                  95

Glu Asn Val Lys Ala Lys Ile Gln Asp Lys Glu Gly Ile Pro Pro Asp
            100                 105                 110

Gln Gln Arg Leu Ile Phe Ala Gly Lys Gln Leu Glu Asp Gly Arg Thr
        115                 120                 125

Leu Ser Asp Tyr Asn Ile Gln Lys Glu Ser Thr Leu His Leu Val Leu
    130                 135                 140

Arg Leu Arg Gly Gly Ser
145                 150
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<210> 30
<211> 143
<212> PRT
<213> Artificial

<220>
<223> H6-TripUB IEPD!TQ

<400> 30

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Met Gly Ser His His His His His His Gly Ser Gly Ser Gly Ser Ile
1               5                   10                  15

Glu Pro Asp Thr Gln Lys Pro Lys Lys Ile Val Asn Ala Lys Lys Asp
            20                  25                  30

Val Val Asn Thr Lys Met Phe Glu Glu Leu Lys Ser Arg Leu Asp Thr
        35                  40                  45

Leu Ala Gln Glu Val Ala Leu Leu Lys Glu Gln Gln Ala Leu Gln Thr
    50                  55                  60
```

```
Val Gly Ser Gln Ile Phe Val Lys Thr Leu Thr Gly Lys Thr Ile Thr
65                  70                  75                  80

Leu Glu Val Glu Pro Ser Asp Thr Ile Glu Asn Val Lys Ala Lys Ile
                85                  90                  95

Gln Asp Lys Glu Gly Ile Pro Pro Asp Gln Gln Arg Leu Ile Phe Ala
            100                 105                 110

Gly Lys Gln Leu Glu Asp Gly Arg Thr Leu Ser Asp Tyr Asn Ile Gln
        115                 120                 125

Lys Glu Ser Thr Leu His Leu Val Leu Arg Leu Arg Gly Gly Ser
    130                 135                 140
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<210> 31
<211> 137
<212> PRT
<213> Artificial

<220>
<223> H6-TripUB IEPD!IV

<400> 31

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Met Gly Ser His His His His His His Gly Ser Gly Ser Gly Ser Ile
1               5                   10                  15

Glu Pro Asp Ile Val Asn Ala Lys Lys Asp Val Val Asn Thr Lys Met
            20                  25                  30

Phe Glu Glu Leu Lys Ser Arg Leu Asp Thr Leu Ala Gln Glu Val Ala
        35                  40                  45

Leu Leu Lys Glu Gln Gln Ala Leu Gln Thr Val Gly Ser Gln Ile Phe
    50                  55                  60

Val Lys Thr Leu Thr Gly Lys Thr Ile Thr Leu Glu Val Glu Pro Ser
65                  70                  75                  80

Asp Thr Ile Glu Asn Val Lys Ala Lys Ile Gln Asp Lys Glu Gly Ile
                85                  90                  95

Pro Pro Asp Gln Gln Arg Leu Ile Phe Ala Gly Lys Gln Leu Glu Asp
            100                 105                 110
```

```
Gly Arg Thr Leu Ser Asp Tyr Asn Ile Gln Lys Glu Ser Thr Leu His
        115                 120                 125

Leu Val Leu Arg Leu Arg Gly Gly Ser
    130                 135
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<210> 32
<211> 150
<212> PRT
<213> Artificial

<220>
<223> H6-TripUB IEPD!EP

<400> 32

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Met Gly Ser His His His His His His Gly Ser Gly Ser Gly Ser Ile
1               5                   10                  15

Glu Pro Asp Glu Pro Gly Thr Glu Pro Pro Thr Gln Lys Pro Lys Lys
            20                  25                  30

Ile Val Asn Ala Lys Lys Asp Val Val Asn Thr Lys Met Phe Glu Glu
        35                  40                  45

Leu Lys Ser Arg Leu Asp Thr Leu Ala Gln Glu Val Ala Leu Leu Lys
    50                  55                  60

Glu Gln Gln Ala Leu Gln Thr Val Gly Ser Gln Ile Phe Val Lys Thr
65                  70                  75                  80

Leu Thr Gly Lys Thr Ile Thr Leu Glu Val Glu Pro Ser Asp Thr Ile
                85                  90                  95

Glu Asn Val Lys Ala Lys Ile Gln Asp Lys Glu Gly Ile Pro Pro Asp
            100                 105                 110

Gln Gln Arg Leu Ile Phe Ala Gly Lys Gln Leu Glu Asp Gly Arg Thr
        115                 120                 125

Leu Ser Asp Tyr Asn Ile Gln Lys Glu Ser Thr Leu His Leu Val Leu
    130                 135                 140

Arg Leu Arg Gly Gly Ser
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145 150

<210> 33
<211> 150
<212> PRT
<213> Artificial

<220>
<223> H6-TripUB IEPD!EG

<400> 33

Met Gly Ser His His His His His His Gly Ser Gly Ser Gly Ser Ile
1 5 10 15

Glu Pro Asp Glu Gly Gly Thr Glu Pro Pro Thr Gln Lys Pro Lys Lys
20 25 30

Ile Val Asn Ala Lys Lys Asp Val Val Asn Thr Lys Met Phe Glu Glu
35 40 45

Leu Lys Ser Arg Leu Asp Thr Leu Ala Gln Glu Val Ala Leu Leu Lys
50 55 60

Glu Gln Gln Ala Leu Gln Thr Val Gly Ser Gln Ile Phe Val Lys Thr
65 70 75 80

Leu Thr Gly Lys Thr Ile Thr Leu Glu Val Glu Pro Ser Asp Thr Ile
85 90 95

Glu Asn Val Lys Ala Lys Ile Gln Asp Lys Glu Gly Ile Pro Pro Asp
100 105 110

Gln Gln Arg Leu Ile Phe Ala Gly Lys Gln Leu Glu Asp Gly Arg Thr
115 120 125

Leu Ser Asp Tyr Asn Ile Gln Lys Glu Ser Thr Leu His Leu Val Leu
130 135 140

Arg Leu Arg Gly Gly Ser
145 150

<210> 34
<211> 37
<212> DNA
<213> Artificial

<220>
<223> TripUB GrB fw primer

<400> 34
gtggatccat cgagcctgac tctcctggta ccgagcc 37

<210> 35
<211> 38
<212> DNA
<213> Artificial

<220>
<223> TripUB GrB rev primer

<400> 35
ggtaccagga gagtcaggct cgatggatcc actaccac 38

<210> 36
<211> 34
<212> DNA
<213> Artificial

<220>
<223> RAP GrB fw primer

<400> 36
cggatccatc gagcctgact actcgcggga gaag 34

<210> 37
<211> 34
<212> DNA
<213> Artificial

<220>
<223> RAP GrB rev primer

<400> 37
cccgcgagta gtcaggctcg atggatccgt gatg 34

<210> 38
<211> 42
<212> DNA
<213> Artificial

<220>
<223> Mut-GrB fw

<400> 38
cgtggtggat ccatcgagcc ggacggtgga gatgaacccc cc 42

<210> 39

<211> 42
<212> DNA
<213> Artificial

<220>
<223> Mut-GrB rw

<400> 39
gggggttca tctccaccgt ccggctcgat ggatccacca cg 42

<210> 40
<211> 33
<212> DNA
<213> Artificial

<220>
<223> TN GrB fw primer

<400> 40
ggatccatcg agcctgacgg cgagccacca acc 33

<210> 41
<211> 33
<212> DNA
<213> Artificial

<220>
<223> TN GrB rev primer

<400> 41
ggctcgccgt caggctcgat ggatccgtga tgg 33

<210> 42
<211> 33
<212> DNA
<213> Artificial

<220>
<223> PC7TripUB GR-AD fw

<400> 42
ggatccatcc aggcagactc tcctggtacc gag 33

<210> 43
<211> 34
<212> DNA
<213> Artificial

<220>
<223> PC7TripUB GR-AD rev

<400> 43
gtaccaggag agtctgcctg gatggatcca ctac 34

<210> 44
<211> 37
<212> DNA
<213> Artificial

<220>
<223> PC7TripUB P-G fw

<400> 44
ggatccatcc aggcagactc tggtggtacc gagccac 37

<210> 45
<211> 38
<212> DNA
<213> Artificial

<220>
<223> PC7TripUB P-G rev

<400> 45
ctcggtacca ccagagtctg cctggatgga tccactac 38

<210> 46
<211> 34
<212> DNA
<213> Artificial

<220>
<223> DNATrip IE-VG fw

<400> 46
gtagtggatc agtcgggcct gactctcctg gtac 34

<210> 47
<211> 34
<212> DNA
<213> Artificial

<220>
<223> DNATrip IE-VG rev

<400> 47
gagagtcagg cccgactgat ccactaccac tacc 34

<210> 48
<211> 31
<212> DNA
<213> Artificial

<220>
<223> DNATrip SP-FG fw

<400> 48
ggcctgactt tggtggtacc gagccaccaa c 31

<210> 49
<211> 31
<212> DNA
<213> Artificial

<220>
<223> DNATrip SP-FG rev

<400> 49
ggctcggtac caccaaagtc aggcccgact g 31

<210> 50
<211> 52
<212> DNA
<213> Artificial

<220>
<223> Trip IEPD-TQ

<400> 50
gggaaaggat ccatcgagcc tgacacccag aagcccaaga agattgtaaa tg 52

<210> 51
<211> 54
<212> DNA
<213> Artificial

<220>
<223> Trip IEPD-IV

<400> 51
gggaaaggat ccatcgagcc tgacattgta aatgccaaga aagatgttgt gaac 54

<210> 52
<211> 39
<212> DNA
<213> Artificial

<220>
<223> UB3

<400> 52
cgcaagcttg catgcttagg atccaccacg aagtctcaa 39

<210> 53
<211> 29
<212> DNA
<213> Artificial

<220>
<223> TripUB EP fw

<400> 53
cgagcctgac gagcctggta ccgagccac 29

<210> 54
<211> 30
<212> DNA
<213> Artificial

<220>
<223> TripUB EP rev

<400> 54
cggtaccagg ctcgtcaggc tcgatggatc 30

<210> 55
<211> 29
<212> DNA
<213> Artificial

<220>
<223> TripUB EG fw

<400> 55
cctgacgagg gtggtaccga gccaccaac 29

<210> 56
<211> 29
<212> DNA
<213> Artificial

<220>
<223> TripUB EG rev

<400> 56
gctcggtacc accctcgtca ggctcgatg 29

<210> 57
<211> 227
<212> PRT
<213> Artificial

<220>
<223> GrB variant C228F

<400> 57

Ile Ile Gly Gly His Glu Ala Lys Pro His Ser Arg Pro Tyr Met Ala
1 5 10 15

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Tyr Leu Met Ile Trp Asp Gln Lys Ser Leu Lys Arg Cys Gly Gly Phe
            20                  25                  30

Leu Ile Gln Asp Asp Phe Val Leu Thr Ala Ala His Cys Trp Gly Ser
        35                  40                  45

Ser Ile Asn Val Thr Leu Gly Ala His Asn Ile Lys Glu Gln Glu Pro
    50                  55                  60

Thr Gln Gln Phe Ile Pro Val Lys Arg Pro Ile Pro His Pro Ala Tyr
65                  70                  75                  80

Asn Pro Lys Asn Phe Ser Asn Asp Ile Met Leu Leu Gln Leu Glu Arg
                85                  90                  95

Lys Ala Lys Arg Thr Arg Ala Val Gln Pro Leu Arg Leu Pro Ser Asn
            100                 105                 110

Lys Ala Gln Val Lys Pro Gly Gln Thr Cys Ser Val Ala Gly Trp Gly
        115                 120                 125

Gln Thr Ala Pro Leu Gly Lys His Ser His Thr Leu Gln Glu Val Lys
    130                 135                 140

Met Thr Val Gln Glu Asp Arg Lys Cys Glu Ser Asp Leu Arg His Tyr
145                 150                 155                 160

Tyr Asp Ser Thr Ile Glu Leu Cys Val Gly Asp Pro Glu Ile Lys Lys
                165                 170                 175

Thr Ser Phe Lys Gly Asp Ser Gly Gly Pro Leu Val Cys Asn Lys Val
            180                 185                 190

Ala Gln Gly Ile Val Ser Tyr Gly Arg Asn Asn Gly Met Pro Pro Arg
        195                 200                 205

Ala Phe Thr Lys Val Ser Ser Phe Val His Trp Ile Lys Lys Thr Met
    210                 215                 220

Lys Arg Tyr
225
```